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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/868,824	09/18/2001	Thomas Wagner	514485-3880	6287

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EXAMINER	
FREDMAN, JEFFREY NORMAN	

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 04/05/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/868,824	WAGNER ET AL.	
	Examiner	Art Unit	
	Jeffrey Fredman	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *February 17, 2004* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *73-128* is/are pending in the application.

4a) Of the above claim(s) *78-80,90,93,96,99,106-108,118,121,123 and 127* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *73-77,81-89,91,92,94,96-98,100-105,109-117,119,120,122,124-126 and 128* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status

1. Claims 73-128 are pending in this action.

Claims 73-77, 81-89, 91, 92, 94, 96-98, 100-105, 109-117, 119, 120, 122, 124-126 and 128 are elected.

Claims 78-80, 90, 93, 96, 99, 106-108, 118, 121, 123, 127 are withdrawn.

Claim Rejections - 35 USC § 112

2. The rejection of claims 73-77, 81-89, 91, 92, 94, 96-98, 100-105, 109-117, 119, 120, 122, 124-126 and 128 under 35 U.S.C. 112, second paragraph, is withdrawn in view of the amendment.

With regard to the term "recognizes" in claim 73, this term can represent any form of recognition, whether hybridization, van der waal's interaction, or covalent linkage for purposes of the prior art.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 73-77, 81-89, 92, 94, 100-105, 109-117, 120, 122, 126 and 128 are rejected under 35 U.S.C. 102(b) as being anticipated by Urdea et al (U.S. Patent 5,635,352).

Urdea teaches a process for detecting a marker in a sample (see abstract) comprising the following steps:

(a) providing a sample comprising a first and a second detectable analyte (see figure 8, where the first detectable analyte is the target nucleic acid and the second detectable analyte is the amplification multimer);

(b) contacting the sample with a first recognition species that recognizes the first marker (See figure 8, where either CE1 or CE2 can comprise the first recognition species);

(c) contacting the sample with a second recognition species that recognizes both the first marker and the second marker (See figure 8, where the label extender (LE) is a second recognition species that recognizes both the first detectable analyte, the target DNA, and the second detectable analyte, the amplification multimer),

(d) contacting the sample with a third recognition species that recognizes the second detectable analyte (see figure 8, where the detector probes hybridize to the amplification multimer and represent the third recognition species); and

(e) detecting the presence of a complex comprising the first, second, and third recognition species (see figure 8 and column 4, lines 2-10, for example).

With regard to claims 74-76, 102-104, Urdea teaches immobilization of the first recognition species by hybridization to a nucleic acid on a solid support where the solid support is a solid and can be composed of plastic (see figure 8, CE2 or CE1 are

hybridized to CP which is immobilized on a solid support and column 19, which exemplifies attachment of the probe to a microtiter plate).

With regard to claims 77, 81, 105, 109,, the first recognition species is DNA (see figure 8 and column 11, lines 18-28).

With regard to claim 82, 110, the interactions between the recognition species involves a non-covalent interaction involving hydrogen bonds, specifically nucleic acid hybridization (see figure 8).

With regard to claim 83, 111, Urdea teaches the third recognition species, the detector probes, are labeled (see column 11, lines 8-17).

With regard to claim 84, 112, Urdea teaches the situation where there are two third recognition species that are coupled to different labels (see figure 13).

With regard to claim 85, 113, Urdea teaches enzymatic labels, as well as other labels (see column 22, line 9).

With regard to claim 86, 114, Urdea teaches signal amplification of the markers (see figure 8, where the amplifier probe binds to multiple detector probes, thereby amplifying the signal derived from the presence of the markers).

With regard to claim 87, 115, Urdea teaches that the method is performed in a competitive manner to ensure specific hybridization (see column 12, lines 31-40, where Urdea expressly teaches that the method is designed to achieve the goal of "reducing the likelihood that incorrect moieties will bind to the support bound capture probes." This clearly shows that there are incorrect moieties competing with the correct moieties).

With regard to claims 88-89, 92, 94, 116, 117, 120, 122, 126, the first marker is a natural nucleic acid and the second marker is an antigen. Further, with regard to the recognition elements, each of these can be natural nucleic acids and can be "hybrids", since any nucleic acid is a hybrid of multiple nucleotides and since there is no definition of what a "hybrid" nucleic acid is in the specification (see figure 8, where an antigen is interpreted broadly as anything which can cause an immune response, including, of course, the nucleic acids in figure 8).

With regard to claim 100, 128, the target nucleic acid of Urdea is a disease marker for Hepatitis C virus (see column 27, lines 3-18).

With regard to claim 101, Urdea teaches additional elements which recognize both the marker and third recognition element (see figure 11, LE1 and LE2).

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 91, 96-98, 119, 124 and 125 are rejected under 35 U.S.C. 103(a) as being unpatentable over Urdea et al (U.S. Patent 5,635,352) as applied to claims 73-77, 81-89, 92, 94, 100-105, 109-117, 120, 122, 126 and 128 above and further in view of Lizardi et al (U.S. Patent 6,143,495).

Urdea teaches a process for detecting a marker in a sample (see abstract) comprising the following steps:

(a) providing a sample comprising a first and a second marker (see figure 8, where the first marker is the target nucleic acid and the second marker is the amplification multimer);

(b) contacting the sample with a first recognition species that recognizes the first marker (See figure 8, where either CE1 or CE2 can comprise the first recognition species);

(c) contacting the sample with a second recognition species that recognizes both the first marker and the second marker (See figure 8, where the label extender (LE) is a second recognition species that recognizes both the first marker, the target DNA, and the second marker, the amplification multimer),

(d) contacting the sample with a third recognition species that recognizes the second marker (see figure 8, where the detector probes hybridize to the amplification multimer and represent the third recognition species); and

(e) detecting the presence of a complex comprising the first, second, and third recognition species (see figure 8 and column 4, lines 2-10, for example).

With regard to claims 74-76, 102-104, Urdea teaches immobilization of the first recognition species by hybridization to a nucleic acid on a solid support where the solid support is a solid and can be composed of plastic (see figure 8, CE2 or CE1 are hybridized to CP which is immobilized on a solid support and column 19, which exemplifies attachment of the probe to a microtiter plate).

With regard to claims 77, 81, 105, 109,, the first recognition species is DNA (see figure 8 and column 11, lines 18-28).

With regard to claim 82, 110, the interactions between the recognition species involves a non-covalent interaction involving hydrogen bonds, specifically nucleic acid hybridization (see figure 8).

With regard to claim 83, 111, Urdea teaches the third recognition species, the detector probes, are labeled (see column 11, lines 8-17).

With regard to claim 84, 112, Urdea teaches the situation where there are two third recognition species that are coupled to different labels (see figure 13).

With regard to claim 85, 113, Urdea teaches enzymatic labels, as well as other labels (see column 22, line 9).

With regard to claim 86, 114, Urdea teaches signal amplification of the markers (see figure 8, where the amplifier probe binds to multiple detector probes, thereby amplifying the signal derived from the presence of the markers).

With regard to claim 87, 115, Urdea teaches that the method is performed in a competitive manner to ensure specific hybridization (see column 12, lines 31-40, where Urdea expressly teaches that the method is designed to achieve the goal of "reducing the likelihood that incorrect moieties will bind to the support bound capture probes." This clearly shows that there are incorrect moieties competing with the correct moieties).

With regard to claims 88-89, 92, 94, 116, 117, 120, 122, 126, the first marker is a natural nucleic acid and the second marker is an antigen. Further, with regard to the recognition elements, each of these can be natural nucleic acids and can be "hybrids", since any nucleic acid is a hybrid of multiple nucleotides and since there is no definition of what a "hybrid" nucleic acid is in the specification (see figure 8, where an antigen is interpreted broadly as anything which can cause an immune response, including, of course, the nucleic acids in figure 8).

With regard to claim 100, 128, the target nucleic acid of Urdea is a disease marker for Hepatitis C virus (see column 27, lines 3-18).

With regard to claim 101, Urdea teaches additional elements which recognize both the marker and third recognition element (see figure 11, LE1 and LE2).

Urdea does not teach the use of antibody as either a recognition species or conjugated to a nucleic acid for detection purposes.

Lizardi teaches conjugation of antibodies to nucleic acids for detection purposes (see figure 9 and column 52, lines 8-31).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use the nucleic acids conjugated to antibodies for detection purposes as taught by Lizardi in the method of Urdea since Lizardi states "By coupling a nucleic acid tag to a specific binding molecule, such as an antibody, amplification of the nucleic acid tag can be used to detect analytes in a sample (see column 3, lines 18-20)". Thus, an ordinary practitioner, motivated by Urdea to amplify the detection of the sample using the amplifier probe, would have been motivated to use the antibody of Lizardi in order to combine the detection of sample analytes with the nucleic acid amplification for detection of a broader range of analytes.

Response to Arguments

8. Applicant's arguments filed February 17, 2004 have been fully considered but they are not persuasive.

Applicant's argument depends upon the definition and understanding of the term "analyte". Applicant argues that while the target in figure 8 of Urdea is admittedly an analyte, Applicant would indicate that the amplification multimer is not an analyte because it is not part of the sample. This is not found persuasive because there is no requirement as to what elements constitute a sample or an analyte. A review of all 14 pages of the specification fails to find any support for the narrow interpretation adopted by Applicant. As Applicant is aware, "During patent examination, the pending claims

must be given their broadest reasonable interpretation consistent with the specification." (see MPEP 2111). Here, the broadest reasonable interpretation of the claims is to read the amplification multimer as an "analyte" since it is being analyzed in the method of figure 8. Further, the "sample" is "provided" when all of the reagents are mixed together, which clearly meets the requirements of step (a). So the distinction being urged by Applicant is not found persuasive because it is not rooted in a structural difference between the claim and the prior art, but rather on a linguistic choice. A person interested in determining how well the method of Urdea would function with a particular analyte "target" would also consider the amplification multimer an "analyte" as well. Therefore the rejection is maintained.

Conclusion

9. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Fredman whose telephone number is (571)272-0742. The examiner can normally be reached on 6:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571)272-0782. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jeffrey Fredman
Primary Examiner
Art Unit 1637